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EXAMINER

RAGHU, GANAPATHIRAM

ART UNIT	PAPER NUMBER
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1652

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12/05/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/761,530

Applicant(s)

KOEBERL ET AL.

Examiner

Ganapathirama Raghu

Art Unit

1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 September 2007.
2a) ☒ This action is FINAL. 2b) ☐ This action is non-final.
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5-8-12, 14-18, 21, 22, 24-73, 75-76 and 79-82 is/are pending in the application.
4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5) ☐ Claim(s) _____ is/are allowed.
6) ☒ Claim(s) 1-5-8-12, 14-18, 21, 22, 24-29, 73, 75-77 and 79-82 is/are rejected.
7) ☐ Claim(s) _____ is/are objected to.
8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 09/24/07
4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____

Application Status

In response to the Office Action mailed on 05/24/2007, applicants' filed a response on 09/24/2007. Said response, amended claims 1, 21, 26, 73, 75, canceled claims 6, 7, 13, 17, 19, 20, 23 74 and 78 and added new claims 80-82. Claims 30-72 remain withdrawn as they are drawn to non-elected inventions, thus claims 1-5, 8-12, 14-18, 21, 22, 24-29, 73, 75-77 and 79-82 are pending in this application and are under consideration.

Objections and rejections not reiterated from previous action are hereby withdrawn.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 09/24/07 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner is considering the IDS statement.

Withdrawn- Claim Rejections: 35 USC § 112-First Paragraph

Claim 1 and claims 2-5, 8-12, 14-18, 21, 22, 24-29, 73, 75-77 and 79 depending therefrom, rejected under 35 U.S.C. 112, first paragraph for enablement and written description, are being withdrawn due to amendments to the claims and persuasive arguments by the applicant.

Maintained-Claim Rejections: 35 USC § 102

Previous rejection of claims 1-2, 5, 8-12, 14-16, 18, 21, 22, 24-29 rejected under 35 U.S.C. 102(b) as being anticipated by Amalfitano et al., (WO 02/098466 A1, 2002, in IDS) when given the broadest interpretation is maintained.

Claims 1-2, 5, 8-12, 14-16, 18, 21, 22, 24-29 are directed to any isolated nucleic acid encoding a chimeric polypeptide comprising a secretory signal sequence, i. e., any human GAA polypeptide and comprising any secretory signal sequence including variants, mutants and

recombinants and further comprising a polynucleotide from any 3' untranslated region, vector comprising said polynucleotides and a pharmaceutical composition comprising said vectors and to a method of delivering said polypeptide. Amalfitano et al., (*supra*) teach adenovirus and adeno-associated virus vectors comprising polynucleotides encoding chimeric polypeptides comprising a secretory signal sequence operably linked to human GAA (lines 13-26, page 22) and a method of producing said polypeptide in many mammalian cultured cells such as CHO, 293 and in vivo in hepatocytes (Summary of the Invention: pages 3-41; especially pages 6, 7, 12, 22, 26, 28-30, 35, 41 and Examples 1, 4, 9, and 13). Therefore, the reference of Amalfitano et al., anticipates claims 1-2, 5, 8-12, 14-16, 18, 21, 22, 24-29 of the present invention.

Previous rejection of claims 1-2, 5, 8-12, 14-16, 18, 21, 22, 24-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Van Bree et al., (WO 00/34451, 2000, in IDS) when given the broadest interpretation is maintained.

Claims 1-2, 5, 8-12, 14-16, 18, 21, 22, 24-29 are directed to any isolated nucleic acid encoding a chimeric polypeptide comprising a secretory signal sequence, i. e., any human GAA polypeptide and comprising any secretory signal sequence including variants, mutants and recombinants and further comprising a polynucleotide from any 3' untranslated region, vector comprising said polynucleotides and a pharmaceutical composition comprising said vectors and to a method of delivering said polypeptide. Van Bree et al., (*supra*) teach compositions comprising polynucleotides encoding the human GAA with native secretory signal sequence and also suggest said GAA can be operably linked to other signal peptides (page 9, lines 16-30), vectors, methods of expression, pharmaceutical composition comprising said polynucleotides

and encoded polypeptides, and a method of producing said polypeptide in many mammalian cultured cells such as CHO, 293 and in vivo in heaptocytes, method of administering said compositions to treat Pompe's disease (GAA deficiency) and methods to generate transgenic animals comprising polynucleotides encoding human GAA (Summary of the Invention: pages 3-28; especially pages 7, 9 and 10). Therefore, the reference of Van Bree et al., anticipates claims 1-2, 5, 8-12, 14-16, 18, 21, 22, 24-29 of the present invention.

In response to the above rejection, applicants have traversed on the basis that:

(A) The claims as now presented require that secretory signal sequence replace the leader sequence of native human GAA. Amalfitano et al., includes no such teaching.

(B) The claims as now presented require that secretory signal sequence replace the leader sequence of native human GAA. Van Bree et al., includes no such teaching. "Applicants, not the art showed that secreted lysosomal proteins (as exemplified by hGAA) demonstrate...unaltered glycosylation and processing of the chimeric protein.

Reply (A) (B): Applicants' arguments have been fully considered but are not deemed persuasive for the following reasons:

At the outset claims as written are not directed to a human GAA wherein unaltered glycosylation and processing of the chimeric protein occurs as a result of replacing the leader sequence of native human GAA with a secretory signal sequence and furthermore the arguments presented below clearly provide evidence that replacing the leader sequence of native human GAA with a secretory signal sequence and demonstration of biological activities in said chimeric proteins were well known in the art, thus implying unaltered glycosylation and correct processing for the maintenance of biological activity.

The concept of replacing the native leader sequence with the signal peptide for the polypeptide of the interest to be secreted into the medium was clearly envisaged and disclosed by Amalfitano et al., See page 22, lines 13-22 "As further alternative, the adenovirus vectors can be used to infect a cell in culture to express a desired gene product, e.g., to produce a polypeptide of interest (for example, lysosomal acid α -glucosidase). Preferably, the polypeptide is secreted into the medium can be purified therefrom using routine technique known in the art. Said reference also provides evidence that the configured recombinant human GAA comprising secretion signal is correctly processed, secreted, biologically active and uptake of the secreted human GAA when administered to mice (Figs: 4A-B and 5A-C; pages 8-9, 31-33; Examples 7-8, pages 50-51; Examples 11-14, pages 54-58). Signal peptide sequences that direct extracellular secretion of proteins are known in the art and nucleotide sequences encoding the same can be operably linked to the nucleotide sequence encoding the polypeptide of interest by routine techniques known in the art. Alternatively, the cells can be lysed and the expressed recombinant protein can be purified from cell lysate. The cell may be bacterial, protozoan, plant, yeast, fungus or animal cell". Further as stated in the above rejection applicants' are referred to pages 3-41; especially pages 6, 7, 12, 22, 26, 28-30, 35, 41 and Examples 1, 4, 9, and 13 in Amalfitano et al., wherein each and every element of the instant invention are disclosed.

Similarly Van Bree et al., in pages 3-28; especially pages 7, 9 and 10 disclose each and every element of the instant invention. Said reference discloses many mammary gland specific signal sequences such as α -lactalbumin, α -casein, β -casein that can be potentially employed as signal sequences for the expression of human GAA transgene, recovery of the expressed polypeptide and use of purified polypeptide for the treatment of patients having genetic or other

deficiency resulting in insufficiency of functional lysosomal GAA enzyme (page 15; Example 3-4, pages 25-28), providing evidence that recombinant GAA comprising heterologous secretion signals are correctly processed and biologically active.

Maintained-Claim Rejections 35 USC § 103

Claims 3-4, 73, 75, 77 and 79-82 are rejected under 35 U.S.C. 103(a) as being anticipated by Amalfitano et al., (WO 02/098466 A1, 2002, in IDS) in view of Heus JH (US Patent No.: 6,858,425 B1, claiming priority date of Application No.: 09/454,466 filed on 12/03/99) and Haseltine et al., (WO 2005/003296 A2, claiming priority date of Application No.: 60/441,305 filed on 01/22/03).

Claims 1-3, 5, 8-12, 14-16, 18, 21, 22, 24-29, 73, 75, 77, and 79-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Amalfitano et al., and Heus JH and further in view of Martin et al., (WO 00/47741, 2000).

Claims 1-3, 5, 8-12, 14-16, 18, 21, 22, 24-29, 73, 75-77, and 79-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Amalfitano et al., and Heus JH and further in view of Whitfield et al., (US Patent No.: 5,298,400, 1994).

Claims 1-3, 5, 8-12, 14-16, 18, 21, 22, 24-29, 73, 75-77, and 79-82 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Amalfitano et al., and Heus and further in view of Meulien P (US Patent No.: 5,521,070, 1996).

In response to the above rejection, applicants have traversed on the basis that:

(A) "Applicants, not the art showed that secreted lysosomal proteins (as exemplified by hGAA) demonstrate...unaltered glycosylation and processing of the chimeric protein.

(B) "The failing of Amalfitano is discussed above (102(b) rejection traversal)" implying in accordance with applicants' arguments, the entire 103 (a) obviousness rejections fall.

Reply: Applicants' arguments have been fully considered but are not deemed persuasive as examiner is not withdrawing the 102(b) rejections and furthermore examiner continues to hold the position that specific teaching, suggestion, motivation and expectation of success are all provided in the cited references for the 103 (a) obviousness rejection. Examiner in support to rebut the applicants' arguments would like to point out that a) an expectation of unaltered glycosylation and processing is not necessary but only an expectation of producing a biologically active GAA and b) there is an expectation of producing biologically active GAA upon secretion in view of showing of biological activity of the secreted GAAs produced by the primary references (i.e., cited prior art).

Summary of Pending Issues

The following is a summary of issues pending in the instant application.

- 1) Previous rejection of claims 1-2, 5, 8-12, 14-16, 18, 21, 22, 24-29 rejected under 35 U.S.C. 102(b) as being anticipated by Amalfitano et al., (WO 02/098466 A1, 2002, in IDS) and Van Bree et al., (WO 00/34451, 2000, in IDS) when given the broadest interpretation is maintained.
- 2) Previous rejection of claims 1-3, 5, 8-12, 14-16, 18, 21, 22, 24-29, 73, 75-77, and 79-82, rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Amalfitano et al., Heus JH, Haseltine et al., Martin et al., Whitfield et al., and Meulien P is maintained.

Conclusion

None of the claims are allowable. Claims 1-3, 5, 8-12, 14-16, 18, 21, 22, 24-29, 73, 75-77, and 79-82 are rejected for the reasons identified in the Rejections and Summary sections of this Office Action. Applicants must respond to the objections/rejections in each of the sections in this Office Action to be fully responsive for prosecution.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Final Comments

To insure that each document is properly filed in the electronic file wrapper, it is requested that each of amendments to the specification, amendments to the claims, Applicants'

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remarks, requests for extension of time, and any other distinct papers be submitted on separate pages.

It is also requested that Applicants identify support, within the original application, for any amendments to the claims and specification.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathirama Raghu whose telephone number is 571-272-4533. The examiner can normally be reached between 8 am-4: 30 pm EST. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of the application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ganapathirama Raghu, Ph.D.

Patent Examiner

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Oct. 30, 2007.

/Rebecca Prouty/

Primary Examiner

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